Diagnosis of Rheumatoid Arthritis Amoung Different Age Groups in Around Kancheepuram District, Tamilnadu

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ABSTRACT *Objective:* To assess the diagnostic utility of anti nuclear antibody (ANA) in rheumatoid arthritis (RA) and compare it with rheumatoid factor (RF). The inflammation rate was estimated by CRP and ESR. To check the sensitivity and specificity of CRP and compare it with ESR. Methodology: A review of medical records of patients presenting to the clinics with complaints of joint pains and swelling and who were tested for their serum ANA and RF was done. Inclusion criteria were presence of clinical synovitis in at least one joint and an absence of alternative diagnosis. Scoring and classification of RA was done using the RA Classification Criteria by the American College of Rheumatology (ACR). Results:. Out of 90 test samples, 50 samples (55.7%) showed RF positivity, 20 samples (22.2%) showed ANA –Ab positivity, 26 samples (65.6%) showed CRP positivity, 51 samples (56.7%) showed ESR positivity. Out of 50 RF positive samples, 16 samples (32%) showed RF and ANA-Ab positive, 47 samples (94%) showed CRP positive and 42(84%) samples showed ESR positive. Conclusion: From the present study we have concluded, that for the detection of RA diagnostic parameters like RF, CRP, ESR play an important role in the early diagnosis of infection

INTRODUCTION

Rheumatoid arthritis is the common systemic autoimmune disease prevalent in around 1% of the world population. It is multifunctional in origin and characterized by the inflammation of the membrane unit joints. Early indicators are swelling and pain of interphangeal and metacarpo joints. The course of the disease is variable but tends to be chronic and characterized by exacerbations and remissions. Most frequently in females than males which suggests that sex hormones are influential in its etiology.

SYMPTOMS OF RHEUMATOID ARTHRITIS INCLUDE (The 1987 ARA CRITERIA)

Morning stiffness: Morning stiffness in and around the points lasting at least 1h before maximal improvement. Arthritis in three or more joint areas: Soft tissue swelling or fluid (not bony overgrowth) observed by a physician, present simultaneously. Arthritis of hand joints: Swelling of wrist, MCP or PIP joints for at least 6 weeks. Symmetric Arthritis: Simultaneous involvement of the same joint areas (defined in 2) on both sides of the body (bilateral involvement of PIP, MCP or MTP joints is acceptable without absolute symmetry) for at least 6 weeks. Rheumatoid nodules: Subcutaneous nodules over bony prominences, extensor surfaces or in juxta-articular regions, observed by a physician. Rheumatoid factor: Detected by a method positive in fewer than 5% of normal controls. Radiographic changes: Typical of RA on poster anterior hand and wrist radiographs; it must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (OA changes alone do not qualify).

A blood test is used to detect the presence of rheumatoid factor. Rheumatoid factor is present in 80% of adults who have rheumatoid arthritis. The incidence of rheumatoid factor increases with the duration of disease in rheumatoid arthritis, at 3 months the incidence is 33%, while at one year it is 75%.

Other autoimmune diseases can also be positive for rheumatoid factor including: Sjogren's Syndrome, Systemic lupus erythematosus, Scleroderma, Polymyositis / Dermatomyositis, Mixed Connective Tissue Disease. Conditions NOT associated with elevated rheumatoid factor include: Osteoarthritis, Ankylosing spondylitis, Gout, Psoriatic arthritis, Reiter's syndrome. High levels or titers of rheumatoid factor are associated with more severe rheumatoid arthritis. This factor also has been associated with a higher tendency to develop the non-joint complications of the disease such as and rheumatoid nodules and rheumatoid lung disease.

Antibodies are protein, produced by WBC's which normally circulate in the blood to defend against foreign invaders such as bacteria, viruses and toxins. Auto antibodies, instead of acting against foreign invaders as normal antibodies do, attack the body's own cells. Antinuclear antibodies are unique group of auto antibodies that have the ability to attack structures in the nucleus of cells. The nuclear of a cells contains genetic material referred to as DNA. There is an ANA test which can be performed on a patients blood sample as part of the diagnostic process to detect certain autoimmune disease. ANA is also known as FANA (fluorescent antinuclear antibody) test. In this method serum from patient blood specimen is added to microscopic slide which have commercially prepared cells on the slide surface. If the patient's serum contains antinuclear antibod-

ies (ANA), they bind to the cells (specifically the nucleus of the cells) on the side. A second antibody, commercially tagged with a fluorescent dye, is added to the mix of patient's serum and commercially prepared cells on the slide. The second (fluorescent) antibody attaches to the serum antibodies and cells which have bound together.

As a blood test, CRP is not specific. A high result serves as a general indication of acute inflammation. In cases of inflammatory rheumatic diseases, such as rheumatoid arthritis and lupus, doctors can utilize the CRP test to assess the effectiveness of a specific arthritis treatment and monitor periods of disease flare up. It's value is as a general indicator, not specific. It must be noted that even in known cases of inflammatory disease, such as rheumatoid arthritis and lupus, a low CRP level is possible, and is not indicative of no inflammation. Normally there is no CRP in blood serum. From Lab Tests Online, "a high or increasing amount of CRP in your blood suggests that you have an acute infection or inflammation. Although a result above 1 mg/dl is usually considered high for CRP, most infections and inflammations result in CRP levels above 10 mg/dl". A positive CRP may be an indicator of several conditions, including: Rheumatoid arthritis, Rheumatic fever, Cancer, Tuberculosis, Pneumonia, Heart attack and Lupus.

Another blood test often ordered in conjunction with CRP is known as ESR (Erythrocyte Sedimentation Rate or Sedrate). Both CRP and ESR give similar information about non-specific inflammation. CRP appears and disappears more quickly than changes in ESR. Therefore, your CRP level may drop to normal following successful treatment, whereas ESR may remain elevated for a longer period. Elevations in both CRP and ESR are associated with radiographic progression at 6 and 12 months can correlate with disease progression over periods of over 20 years. However, studies also show that progressive joint damage occur despite improvement in CRP. Thus, the CRP alone cannot dictate treatment. In the present study focus has been made on the diagnosis of RA among different age & sex groups by serological and haematological parameters like RF, ANA, CRP & ESR and to correlate RA with the above serological and haematological tests.

MATERIALS AND METHODS

Total of 90 Samples were collected from RA suspected patients and patients currently diagnosed with arthritis according to revised American College of Rheumatism (ACR criteria) and 10 apparently healthy subjects as control group in the Department of Rheumatology, Hindu Mission Hospital, Tambaram west, Chennai, Tamil Nadu. 5ml of blood was collected aseptically by vein puncture from the test patient and from healthy individuals. The samples were then categorized into 3 different groups based on the age. Each group contains 30 test samples & 10 control samples. The three groups were as follows: Group I (1 –30 Years), Group II (30 – 60 Years) and Group III (60 –90 Years).

Serum RF, CRP was analyzed by Neplometry on Mispa i2 (Agappe Diagnostics). The system was closely monitored by routine practice of running both high and low controls with every batch analyzed. The normal positive significant value of RF = 0 - 20 IU/L. Values of CRP greater than 1 mg/dl were considered abnormal.

Serum ANA was assayed (using a QUANTA Lite ANA ELISA assay kit, INOVA DIAGNOSTICS, CA, USA) by Enzyme Linked Immuno Sorbent Assay on Semi-automated Microplate ELISA reader, LISAQUANT-TS (TULIP GROUP). Positive and Negative controls provided by the manufacturer (QUANTA Lite ANA ELISA assay kit, INOVA DIAGNOSTICS, CA, USA) were run with every batch analyzed. The measuring range of the assay was 7 – 500 U/ml. Samples with ANA concentrations above the measuring range were diluted 1:2 to 1:5 manually. Levels of ANA < 1.0 Index Value were considered normal, 1.0-1.2 Index Value as Moderate positive and values > 1.2 Index Value as high-level positive.

Erythrocyte sedimentation rate was measured using the Westergren method. The system for ESR was monitored by two point calibration. 1.6 ml of whole blood was taken and 0.4ml of 3.8% trisodium citrate was added in a clean test tube and the contents were mixed well. It was then loaded in a westergren tube up to '0' mark level. The westergren tube was then fixed in ESR Stand and the red cell sedimentation rate was observed after 1 hour. Values of ESR greater than 20 and 15 mm/hour were considered abnormal for females and males respectively.

RESULTS & DISCUSSION

A total of 90 serum samples were collected from test patients and 30 Serum Samples were collected from normal health individuals

TABLE 1 - SEX WISE DISTRIBUTION OF RF POSITIVITY:

Groups	Total No. of Samples	No. of Samples		Percentage of RF Positives		Percentage of ANA Positives		Percentage of CRP Positives		Percentage of ESR Positives	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Group I	30	12	18	8%	61.1%	8%	11%	25%	55.6%	33.3%	20%
Group II	30	11	19	18.2%	78.9%	9%	47.3%	27.3%	89.5 %	36.3%	73.7 %
Group III	30	7	23	28.6%	82.6%	0%	30.4%	57.1%	95.7%	71.4%	78.3%
TOTAL	90	30	60	16.6%	75%	6.7%	30%	33.3%	81.7%	43.3%	63.3%

Table.1. shows the data of RF, ANA-Ab, CRP and ESR positivity among male and female. From the above table it was inferred that females showed high percentage RF (75%), ANA (30%), CRP (81.7%) and ESR (63.3%) positivity when compared to males. Among the three groups, Group III females showed a high percentage (82.6%) of RF, (47.3%) of ANA – Ab, (97.5%) of CRP and (78.3%) positive when compared to others.

Total of 30 samples were taken from normal healthy persons as controls. 10 samples were taken from each group. Of these all were RF negative. Of these, group I & II were ANA -Ab negative and Group III males showed 20% and females showed 20% positive for ANA – Ab test. Of these, group I showed negative for CRP. Group II males showed 40% and females showed 40% CRP positive and Group III males showed 20%(1) and females showed 60% (3) CRP positive, which is indicative of inflammatory reaction caused by some other clinical manifestations. Of these, group I were negative for ESR. Group II males showed 20%(1) positive for ESR and females showed negative for ESR and Group III males showed 20% (1) and females showed 40% (2) positive for ESR, which is indicative of inflammatory reaction caused by some other clinical manifestations.
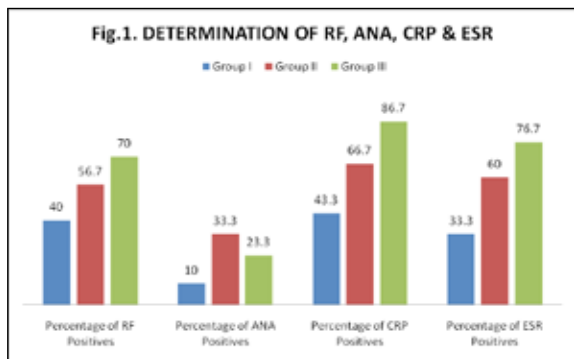

Fig.1. Shows the overall percentage of the diagnostic parameters used in this study. It was inferred that group III individuals showed more sensitivity towards RA which is indicative from their high RF positive (70%), CRP positive (86.7%), and ESR positive (76.7%) values. Among the 90 samples investigated, RF positivity was found to be 55.7%, ANA - Ab positivity was found to be 22.2%, CRP positivity was found to be 65.6% and ESR positivity was found to be 56.7%.

Total of 30 samples were taken form normal healthy person controls. 10 samples were taken from each group. In RF, ANA, CRP, ESR were negative in group I. Group II individuals showed negative value for RF and ANA – Ab but were positive for CRP (40%) and ESR (10%).Group III individuals showed negative for RF and were positive for ANA – Ab (20%), CRP (40%) and ESR (80%).

Groups	No. of RF Positives	Percentage of RF & ANA Positives	Percentage of RF Positives & ANA Negatives	Percentage of RF & CRP Positives	Percentage of RF Positives & CRP Negatives	Percentage of RF & ESR Positives	Percentage of RF Positives & ESR Negatives
Group II	17	47.1%	52.9%	94.1%	5.9%	76.5%	23.5%
Group III	21	14.3%	85.7%	100%	0	90.5%	9.5%
Total	50	32%	68%	94%	6%	84%	16%

Table 2. Shows the co-relation of RA by RF with ANA – Ab, CRP and ESR. From the above table it was inferred that among the three groups, group III individuals showed high percentage of (85.7%) ANA – Ab negative, which in turn indicates that they were more prone to RA. Whereas group II individuals showed high percentage of (47.1%) ANA positive, which indicates that they could suffer from both RA & SLE infections. Out of 50 RF positive samples, 32% (16) showed ANA – Ab positive and 68% (34) showed ANA – Ab negative.

The co-relation of RA by RF & CRP. It was inferred that among the 3 groups, Group III individuals scored high percentage of (100%) CRP positive which in turn indicates that RA patients were more prone to inflammation which is accompanied by more amount of IgM Ab production. Where as group I individuals showed high percentage of (16.7%) CRP negative which is indicative of RA positivity but without any symptoms of inflammation and this is seen only during the early stage of infection. Out of 50 RF positive samples 94% (47) showed positive for CRP and 6% showed negative for CRP.

The co-relation of RA by RF & ESR. It was observed that group III individuals showed high percentage of (90.5%) ESR positive, which is indicative of RA. Whereas group II individuals showed a high percentage of (23.5%) RA positivity without any inflammatory response. Out of 50 RF positive samples, 84% (42) of the sample showed positivity to ESR and 16% (8) were ESR negative.

Total of 30 samples were taken from normal healthy persons as controls. 10 samples were taken from each group. Of these all were RF, ANA – Ab, CRP, & ESR negative.
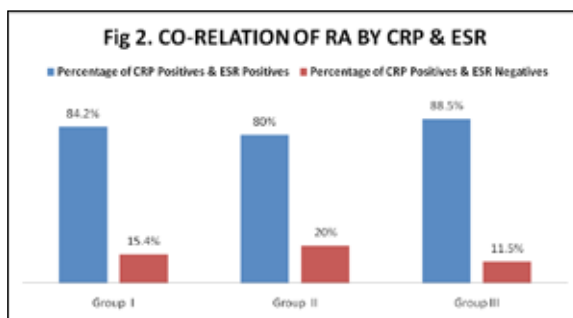

Fig. 2. Shows the correlation of RA by CRP and ESR. From the above table it was inferred that out of 59 CRP positive samples, 50 samples (88.5%) showed ESR positivity and 9 samples (15.2%) showed ESR negativity which in turn indicate CRP is a highly sensitive test when compared to ESR in the diagnosis of active disease.

TABLE 2. CO-RELATION OF RA BY RF, ANA – Ab, CRP & ESR

Groups	No. of RF Positives	Percentage of RF & ANA Positives	Percentage of RF Positives & ANA Negatives	Percentage of RF & CRP Positives	Percentage of RF Positives & CRP Negatives	Percentage of RF & ESR Positives	Percentage of RF Positives & ESR Negatives
Group I	12	41.7%	58.3%	83.3%	16.7%	83.3%	16.7%

TABLE 3. AGE WISE & SEX WISE DISTRIBUTION OF RA

Groups	Total No. of Samples			Percentage of RF, ANA, CRP, ESR Positives		Total	Percentage
	Total	Males	Females	Males	Females		
Group I	30	12	18	1 (8.3%)	9 (50%)	10	33.33%
Group II	30	12	19	1 (9.1%)	12 (63.2%)	13	43.32%

				2	18		
Group III	30	7	23	2 (28.6%)	18 (78.3%)	20	66.78%
TOTAL	90	30	60	4 (13.3%)	39 (65%)	43	47.80%

Table.3. Shows the distribution of RA patients among different age and sex groups. From the above table it was inferred that out of 90 samples collected 43 samples were RF, CRP & ESR positive indicating 48% RA patients. Among the three group, group III 66.78% (20) individuals were more prone to RA and in general females 65% (39) were more affected by RA when compared to males 13.3% (4).

DISCUSSION

According to Ward MM, et al., (2004) out of 88 patients, 54.5% were RF positive, 25% were ANA positive, 55.7 % were CRP Positive and 49.7% were ESR positive. In our present work it was found out that 55.7% were RF positive, 23.2% were ANA positive, 65.6% were CRP positive and 56.7% , were ESR positive, which in turn correlates well with the above report. According to Shin Ys, et al., (2005) in his studies he has found out that out of 104 RF positive patients, 37.5% were ANA positive and Samani N et al., (2005) has observed low levels of ANA among RA patients when compared to SLE patients. In our study, it was found out that out of 50% RF positive patients, 32% were ANA positive, which is found to be comparable with the above report. Nur Mohamed MT et al., (2005) has observed that out of 48 RF positive patients, 84% were CRP positivity. Nikolaisen C, et al., (2005) in his study has found that out of 146 RA patient, 135 (92.5%) were CRP positive. Nielson MM. et al., (2004) has measured CRP levels in sera of 111 RA positive and has found out 107 (96.4%) were CRP positive. In our work it was found out that, out of 50 RF positive patients, 47 (94%) were CRP positive. Mafsude Y, et al., (2004) reported that out of 118 RF positive patients, 86% were ESR positive. Mu R. et al., (2005) detected CRP levels in sera of 99 RA patients and has found out 84 (84.8%) were ESR positive. In our study it was found out that out of 50 RF positive patients, 84.7% were ESR positive. Samani, et al., (2005) compared serum CRP and ESR in 241 patient with RA and has found out that out of 241 RA patients, 92.9% were CRP positive and 86.7% er ESR positive. Chen HA, et al., (2006) has detected CRP levels and ESR in 56 RA positive patients, out of which 47 (84 %) were CRP positive and 42 (75%) were ESR Positive. In our work it was found out that out of 50 RF positive patients, 94% were CRP positive and 84% were ESR positive. Deborah Gesensway., et al., (2001) reported that the disease can occur in any age but the peek incidence of the disease outset is about 60 years of the age. In his study he has tested 42 patients and has found out 59% females and 45% males were positive for all RF, CRP and ESR test. Gold batt et al., (2005) reported that out of 74 patients, 80% females and 24% males were positive for RA. He also revealed that disease activity increases with increase in age (above 60 years). From our present work, it was inferred that females showed high percentage (65%) of RA positivity when compared to males (13.3%) and group III individuals (60-90 years) showed an increased disease activity (66.78%) when compared to other groups which correlates well with the above report.

CONCLUSION

From the present study we have concluded, RF, CRP, ESR play an important marker in the early diagnosis of Rheumatoid arthritis. We have also found out that, severe the disease condition the more the inflammation and this was indicative from tests like CRP and ESR. This is because CRP is nonspecific and its level can increase in any other inflammatory conditions also whereas RA factor is more specific and can be detectable in serum only in conditions of Rheumatoid Arthritis. We have also found out that distribution of RA is more prominent among females when compared to males.

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